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DEPARTMENT OF REGULATORY AFFAIRS 2904 5 AUG -8 A9:25

1 DNA Way MS#242
South San Francisco, CA 94080-4990
(650) 225-1558
FAX: (650) 467-3198

August 5, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Subject: **Docket number 2005D-0062**
Comments on FDA's Drug Watch for Emerging Drug Safety
(DRAFT GUIDANCE)

Dear Dockets Management Branch:

Enclosed are comments, provided by Genentech, for the Draft Guidance FDA's Drug Watch for Emerging Drug Safety

Thank you for providing us the opportunity to comment on this Draft Guidance. We hope that you will find our comments useful and constructive.

Genentech supports the Agency's efforts to improve the US drug safety system, and we agree that the FDA should communicate important, evidence-based safety information to public in a timely fashion. We share the FDA's commitment to protecting the public health while we work to discover, develop, manufacture and commercialize medicines that address significant unmet medical needs. We are concerned, however, that there are issues embedded in the Drug Watch proposal that have not been fully explored, and we raise some of those issues here. We look forward to participating in the process.

If you have any questions regarding this submission, please contact Michelle Tallin, Associate Director, Regulatory Affairs at (650) 225-6098.

Sincerely,

for Robert L. Garnick, Ph.D.
Senior Vice President
Regulatory Affairs, Quality,
and Compliance

2005D-0062

C11

Docket-024

Draft Guidance for Review and Comment

Draft Guidance for Industry
FDA's Drug Watch for Emerging Drug Safety

Docket No. 2005D-0062

Issued for Comment 10-May-05
Comments due 08-Aug-05

Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080-4990

General Comments

In the Draft Guidance, FDA states that the program's goal is to "share emerging safety information before we [FDA] have fully determined its significance or taken final regulatory action so that patients and healthcare professionals will have the most current information concerning the potential risks and benefits of a marketed drug product upon which to make individual treatment choices" (Guidance, page 2). As proposed, the Drug Watch web site does fulfill its goal as patients and healthcare professionals (HCPs) are not provided the balanced safety and efficacy information needed to make informed healthcare decisions.

We agree that benefit-risk decision making could be aided by quick access to current, verified and reliable information (on both benefit and risk) upon which to base treatment decisions. However, we have concerns that posting only preliminary safety alerts on the Drug Watch web site before their significance is fully determined has the potential to mislead physicians and patients.

Disseminating preliminary, "emerging" information while FDA is "attempting to assess the meaning" (Guidance, page 1), and before its significance is fully determined is inconsistent with the Agency's historic science-based policies. To appreciate the sense of subjectivity and unreliability of the safety data FDA proposes to post on Drug Watch, it is useful to consider what FDA would think about posting preliminary, emerging, positive information about a drug. FDA would never post a single case, or a series of cases, of unexpectedly better news about the safety of a drug. The Agency would not release preliminary efficacy information on a drug to its web site, or allow that data in a label. This incongruity between what FDA proposes to say about potentially negative versus positive news is inconsistent with the stated goal of Drug Watch, which is to provide HCPs and patients the most current information concerning the potential risks and benefits of a marketed drug product.

We recognize that posting possible safety alerts on Drug Watch is intended to help restore confidence in the drug development and post-approval process; however, what is needed most is more benefit-risk education. FDA is proposing to include only negative safety information on the Drug Watch site. On the other hand, when companies issue press releases of new clinical trials data, there is always a requirement to disclose both efficacy and safety findings. If the FDA moves forward with the Drug Watch web site, consideration should be given to incorporating links to the prescribing information for full disclosure of risks and benefits. If this approach is not accepted, then appropriate benefit-risk statements should be included along with the posted safety information such as: "Currently, the benefits of Drug X are expected to outweigh potential risks in properly selected patients for which Drug X is approved."

The criteria FDA is proposing to use to decide which safety issues to post on Drug Watch are not well defined in the guidance document and appear somewhat subjective. As currently written, the draft guidance implies that the Drug Safety Oversight Board may decide what information to post without input from independent experts or the sponsor. Putting aside whether the FDA has the authority to do this, we believe this approach is inconsistent with the Agency's prior call for more stakeholder collaboration. The sponsor has extensive information and expertise on the safety and benefit profiles of its drugs. Working with the in-house experts of the drug sponsor and independent experts (if necessary) will enhance the quality of any safety information posted on the Drug Watch web site.

If the FDA moves forward with the Drug Watch web site, we recommend that clear, objective criteria for posting safety information be developed. We believe there should be facts or evidence supporting a causal or contributory relationship to product exposure before any type of

"alert" is made public. Criteria such as those proposed by Miller et al (2000) for attribution analyses or other criteria should be considered. In addition, we believe the standard for posting evidence-based safety information on the Drug Watch web site should be high (e.g., the type of information that after a full risk and benefit analysis would warrant a black box warning or product withdrawal). The best use of the Drug Watch web site would be for FDA to post information after it has made a final determination that a black box warning or other significant label change should be made. At that point, FDA could publish the information so that HCPs and patients have the information while the label is being changed and the new label disseminated. This would provide HCPs and patients with carefully vetted information upon which to base treatment decisions

The Draft Guidance states that the FDA intends to notify relevant sponsors that information about their drugs will be placed on the Drug Watch web site shortly before posting. This approach prevents the opportunity for sponsors to contribute important information that could be useful to the Agency's decision making. For example, a sponsor may have already conducted a thorough evaluation of the safety signal being posted and adequately refuted a causal or contributory association. FDA should want to know that information. In addition, informing sponsors just shortly before posting safety information does not allow sponsors to be prepared for responding to questions from HCPs, patients, and the media.

If the FDA moves forward with the Drug Watch web site, we recommend that sponsors be informed of the Agency's intent to post safety information concerning their products at least two weeks before it is made public. Ideally, the Agency should collaborate with sponsors and independent experts (if necessary) to evaluate potential safety signals well before any public statements are issued.

The Draft Guidance indicates that the FDA intends to update information posted on the web site frequently as new information becomes available or specific issues are resolved; however, the criteria and process for removing safety alerts from the web site are not well defined. We have concerns that if unreliable data are posted on Drug Watch and later retracted, HCPs and patients will remain misinformed without a process for corrective follow-up communications. Adding to our concern, there does not appear to be a mechanism to rapidly inform the public of false alarms.

If FDA posts a potential safety alert on Drug Watch, it should also provide information on the extent of exposure, expected event rates, and the number of events reported to put the safety signal into proper perspective for HCPs and patients. It should follow-up that posting with updated information as the assessment continues and then publish its final review. The final review should describe analyses performed and evidence-based conclusions. FDA should also state what, if any, change was made to the label of the drug. Once FDA posts "emerging" information on "potential" risks, it has assumed a duty to the public to update information on the safety or effectiveness of the products promptly as soon as new or more accurate information becomes available.

Given the complexity of safety information and the known problem of "health information illiteracy," we recommend that Drug Watch include interpretation guidance to help those who do not have the necessary clinical or analytical background to understand the relative significance of posted information. Supporting data on drug classes and diseases may aid patient comprehension of the data. To maintain the primary purpose of posting the safety information, wording should be included on the Drug Watch web page that the information posted is not intended to be used in any legal proceeding to establish liability for a claim or injury.

We are also concerned that, as is currently being contemplated, the "Drug Watch" website and the program to rapidly communicate uncertain, emerging safety information, may violate the Federal Data Quality Act, section 515 of the Treasury and General Government Appropriations Act of 2001 (Pub.L. 106-544, H.R. 5658). That Act was passed to limit "regulation by information" and requires the FDA to disseminate only information that adheres to the Act's quality, objectivity, utility, and integrity standards and to the Office of Management and Budget's and Department of Health and Human Services' guidelines. We think that the information potentially disseminated on the Drug Watch web site will be "influential" in that it will have a clear and substantial impact on important private sector decisions – such as whether to prescribe or take a drug. We are concerned that the FDA's proposed safety alerts will not meet the utility and objectivity standards, in that the preliminary information will not be useful to either health care providers or patients, and the preliminary information will not be accurate, clear, complete, and unbiased. In addition, the Drug Watch guidance document does not address the issue of how persons can legally challenge the information posted. For these reasons, FDA should reconsider the Drug Watch web site and program in light of the Drug Quality Act standards.

If our shared goal is to identify, review and communicate confirmed new safety information to health care providers and patients as soon as possible, a more effective approach might be for the FDA, sponsors and independent experts (if necessary) to actively collaborate to identify and evaluate safety signals and, if confirmed, work together to develop the most appropriate risk minimization action plan. For example, if the FDA identifies a potentially important safety signal before a sponsor does, the sponsor should be informed of the finding and a plan (with timeline) for a thorough evaluation. Thereafter, it is understood that the FDA reserves final decision-making authority over what gets posted on the Drug Watch web site. Following such a process would ensure that all available data are evaluated by persons knowledgeable of the safety data, and would provide sponsors sufficient time to prepare for possible posting of new safety information on the Drug Watch web site. This process can be carried out in a short period of time without undue delay of the disclosure of important, evidence-based and useful information to the public.

Conclusion

Genentech appreciates the opportunity to comment on the draft Drug Watch proposal. We hope our comments and recommendations will be considered before a final decision about Drug Watch is made.

Genentech shares the FDA's commitment to patient safety. In this regard, we welcome the opportunity to continue to work with the agency to optimize pharmacovigilance and risk management.

REFERENCE

Miller FW, Hess EV, Clauw DJ, Hertzman PA, Pincus T, Silver RM, et al. Approaches for identifying and defining environmentally associated rheumatic disorders. Arthritis Rheum 2000;43:243–9.